

# **EXHIBIT 45**

**Amendment As A Submission Under 37 C.F.R. § 1.114(c)**

Submitted: September 24, 2009

**Serial No. 10/759,841**

Filed: January 15, 2004

Applicants: Michael Wayne Graham et al.

<b>Form PTO-1449 (Substitute) U.S. Department of Commerce Patent and Trademark Office</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> (Use several sheets if necessary)	<b>Application Number</b>	10/759,841
	<b>Filing Date</b>	January 15, 2004
	<b>First Named Inventor</b>	Michael Wayne Graham
	<b>Art Unit</b>	1635
	<b>Examiner Name</b>	Whiteman, Brian A.
	<b>Attorney Docket No.</b>	0687/74768-AA /JPW/GJG/MJP

### U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Document Number Number-Kind Code <sup>2</sup> (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
	1	5,017,488	05-21-1991	McAllister et al.
	2	5,270,163	12-14-1993	Gold et al.
	3	5,457,189	10-10-1995	Crooke et al.
	4	5,580,703	12-03-1996	Kotin et al.
	5	5,707,835	01-13-1998	Haseloff et al.
	6	5,795,715	08-18-1998	Thierry Livache et al.
	7	6,344,316 B1	02-05-2002	David J. Lockhart et al.
	8	6,995,258	02-07-2006	Rossietal et al.
	9	2003/0148519	08-07-2003	Engelke et al.

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	10	Amendment submitted June 12, 2008 in connection with U.S. Serial No. 11/593,056, filed November 6, 2006	
	11	Office Action issued September 12, 2008 in connection with U.S. Serial No. 11/593,056, filed November 6, 2006	
	12	Advisory Action issued June 6, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	13	Advisory Action issued June 6, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	14	Amendment submitted May 11, 2009 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	15	Amendment submitted September 2, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	16	Amendment, including Exhibits A and B submitted May 21, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	17	Communication submitted September 2, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	18	Final Office Action issued August 13, 2009 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	19	Interview Summary for February 1, 2008 Interview in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	20	Office Action issued July 30, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	
	21	Office Action issued November 10, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	

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	22	Amendment and Request for Continued Examination submitted January 7, 2009 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	
	23	Final Office Action issued May 15, 2009 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	
	24	Notice of Improper Request for Continued Examination issued October 29, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	
	25	Office Action issued July 7, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	
	26	Request for Continued Examination submitted October 7, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	
	27	Amendment submitted October 9, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	
	28	Interview Summary for December 22, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	
	29	Interview Summary for February 12, 2009 Interview in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	
	30	Office Action issued January 22, 2009 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	
	31	Office Action issued January 6, 2009 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	
	32	Office Action issued July 9, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	
	33	Amendment and Request for Continued Examination Submitted September 5, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	

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	34	Amendment submitted May 4, 2009 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	
	35	Amendment, including Exhibits A to C submitted September 5, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	
	36	Notice to the applicant regarding a non-compliant or non-responsive amendment issued September 4, 2009 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	
	37	Office Action issued November 3, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	
	38	Office Action issued September 2, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	
	39	Amendment submitted June 6, 2008 in connection with U.S. Serial No. 11/180,928, filed July 13, 2005	
	40	Amendment submitted February 7, 2008 in connection with U.S. Serial No. 10/821,710, filed April 8, 2004	
	41	Notice of Abandonment issued December 15, 2008 in connection with U.S. Serial No. 10/821,710, filed April 8, 2004	
	42	U.S. Published Application No. 2006/0014715, published January 19, 2006 (U.S. Serial No. 11/218,999, filed September 2, 2005; Michael Wayne Graham et al.), including complete file history	
	43	Amendment submitted June 17, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	
	44	Amendment submitted March 30, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	
	45	Communication issued May 21, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	

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	46	Office Action issued May 21, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	
	47	Office Action issued September 30, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	
	48	Response to Communication submitted June 22, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	
	49	Supplemental Response To March 30, 2009 Amendment Filed In Response To September 30, 2008 Office Action filed August 4, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	
	50	Amendment submitted July 15, 2009 in connection with U.S. Serial No. 10/646,070, filed July 13, 2005	
	51	Amendment submitted July 24, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003	
	52	Amendment submitted May 11, 2009 in connection with U.S. Serial No. 10/646,070, filed July 13, 2005	
	53	Amendment submitted October 10, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003	
	54	Amendment, including Exhibits A to I submitted July 24, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003	
	55	Office Action issued November 4, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003	
	56	Office Action, issued June 9, 2009 in connection with U.S. Serial No. 10/646,070, filed July 13, 2005	
	57	Office Action issued July 8, 2008 in connection with U.S. Serial No. 09/646,807, filed December 5, 2000	

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	58	Petition For Extension of Time submitted April 22, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	59	Advisory Action issued April 24, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	60	Advisory Action issued March 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	61	Advisory Action issued March 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	62	Amendment after Final submitted February 26, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	63	Amendment submitted July 11, 2008 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	64	Amendment submitted November 28, 2007 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	65	Appeal Brief submitted July 27, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	66	Decision on Petition For Extension of Time issued April 27, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	67	Decision on Petition Under 37 C.F.R. § 1.181 issued April 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	68	Declaration of Dr. Arthur Riggs Under Under 37 C.F.R. §1.132, including Exhibits A to I submitted February 26, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	69	Interview Summary issued February 12, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	

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	70	Interview Summary issued June 12, 2008 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	71	Office Action issued November 19, 2008 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	72	Office Action issued November 26, 2008 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	73	Petition Under 37 C.F.R. § 1.181 submitted April 3, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	74	Petition Under 37 C.F.R. § 1.182 submitted April 3, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	
	75	Amendment submitted December 19, 2008 in connection with U.S. Serial No. 10/571,384, filed June 1, 2006	
	76	Amendment submitted July 15, 2009 in connection with U.S. Serial No. 10/571,384, filed June 1, 2006	
	77	Office Action issued January 15, 2009 in connection with U.S. Serial No. 10/571,384, filed June 1, 2006	
	78	Office Action issued June 19, 2008 in connection with U.S. Serial No. 10/571,384, filed June 1, 2006	
	79	Pending claims for U.S. Serial No. 10/282,996, filed October 30, 2002	
	80	Pending claims for U.S. Serial No. 10/283,190, filed October 30, 2002	
	81	Pending claims for U.S. Serial No. 10/283,267, filed October 30, 2002	

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	82	Pending claims for U.S. Serial No. 11/826,385, filed July 13, 2007	
	83	Pending claims for U.S. Serial No. 11/905,368, filed September 28, 2007	
	84	Pending claims for U.S. Serial No. 11/905,449, filed October 1, 2007	
	85	U.S. Patent Publication No. 2008/0248576 A1, published October 9, 2008 (Andrew Fire et al.)	
	86	U.S. Patent Publication No. 2003/0051263 A1, published March 13, 2003 (Andrew Fire et al.)	
	87	U.S. Patent Publication No. 2003/0055020 A1, published March 20, 2003 (Andrew Fire et al.)	
	88	U.S. Patent Publication No. 2008/0050342 A1, published February 28, 2008 (Andrew Fire et al.)	
	89	U.S. Patent Publication No. 2008/0081373 A1, published April 3, 2008 (Andrew Fire et al.)	
	90	U.S. Serial No. 11/905,368, filed September 28, 2007 (Andrew Fire et al.)	
	91	Amendment submitted March 19, 2009 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	
	92	Amendment submitted May 1, 2008 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	
	93	March 18, 2009 Declaration Under 37 C.F.R. 1.131 including Annexes I to III, of Dr. Michael Metzloff in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	
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	94	May 1, 2008 Declaration Under 37 C.F.R. § 1.131, including Exhibits 1 to 5 of Peter Michael Waterhouse, Michael Wayne Graham, Ming-Bo Wang and Neil A. Smith in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	
	95	May 7, 2008 Declaration Under 37 C.F.R. 1.132 of Peter Robert Schofield Resubmission in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	
	96	November 1, 2007 Declaration Under 37 C.F.R. § 1.131, including Exhibits 1 to 5 of Dr. Elizabeth Salisbury Dennis in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	
	97	Office Action issued May 11, 2009 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	
	98	Office Action issued September 19, 2008 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	
	99	Amendment submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	
	100	Amendment submitted July 2, 2008 in connection with U.S. Serial No. 11/364,183, filed March 1, 2006	
	101	Declaration by Dr. Michael Metzlauff Under 37 C.F.R. § 1.132 submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	
	102	Declaration of Geoffrey Ellacott submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	
	103	Declaration of Neil Smith submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	
	104	Declaration of Peter Michael Waterhouse submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	
	105	Examiner Interview Summary Record (PTOL - 413) issued August 12, 2009 in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	

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	106	Interview Summary from February 11, 2009 Interview in connection with U.S. Serial No. 11/364,183, filed March 1, 2006	
	107	July 2, 2008 Declaration Under 37 C.F.R. § 1.131, including Exhibits 1 to 3 of Peter Michael Waterhouse, Michael Wayne Graham, and Ming-Bo Wang in connection with U.S. Serial No. 11/364,183, filed March 1, 2006	
	108	Notice to the applicant regarding a non-compliant or non-responsive amendment issued July 9, 2009 in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	
	109	Suggestion of Interference Pursuant to 37 C.F.R. § 41.202, submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	
	110	Supplemental Response or Supplemental Amendment submitted August 10, 2009 in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	
	111	Amendment submitted January 30, 2009 in connection with U.S. Serial No. 11/607,062, filed December 1, 2006	
	112	Office Action issued July 31, 2008 in connection with U.S. Serial No. 11/607,062, filed December 1, 2006	
	113	Office Action issued May 12, 2009 in connection with U.S. Serial No. 11/607,062, filed December 1, 2006	
	114	Amendment submitted January 16, 2008 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007	
	115	Amendment submitted July 6, 2009 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007	
	116	Non-Final Rejection issued August 12, 2009 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007	
	117	Notice of Publication issued May 1, 2008 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007	

<b>EXAMINER SIGNATURE</b>	<b>DATE CONSIDERED</b>
---------------------------	------------------------

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<b>Form PTO-1449 (Substitute) U.S. Department of Commerce Patent and Trademark Office</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> (Use several sheets if necessary)	<b>Application Number</b>	10/759,841
	<b>Filing Date</b>	January 15, 2004
	<b>First Named Inventor</b>	Michael Wayne Graham
	<b>Art Unit</b>	1635
	<b>Examiner Name</b>	Whiteman, Brian A.
	<b>Attorney Docket No.</b>	0687/74768-AA /JPW/GJG/MJP

### NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	118	Restriction Requirement issued May 4, 2009 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007	
	119	European Search Report mailed June 3, 2005, for EP 04015041, filed March 19, 1999, 4 pages	
	120	International Search Report mailed on May 10, 1999, for PCT patent application no. PCT/AU99/00195 filed March 19, 1999, 3 pages	
	121	International Search Report mailed on May 10, 2001, for PCT patent application no. PCT/AU01/00297 filed March 16, 2001, 2 pages	
	122	Third party observations under article 115 EPC against European Patent Application EP 98964202.0 in the name of Carnegie Institution of Washington, submitted to the European Patent Office on March 24, 2009.	
	123	Written Opinion mailed on April 17, 2004, for PCT application no PCT/AU03/01177 filed September 9, 2003, 7 pages	
	124	Bhargava A., et al. (2002) "Glucocorticoids prolong Ca(2+) transients in hippocampal-derived H19-7 neurons by repressing the plasma membrane Ca(2+)-ATPase-1" Mol Endocrinol. 16(7):1629-37	
	125	Bhargava A., et al. (2004) "Long double-stranded RNA-mediated RNA interference as a tool to achieve site-specific silencing of hypothalamic neuropeptides" Brain Res Brain Res Protoc. (2):115-25	
	126	Diallo M., et al. (2003) "Long endogenous dsRNAs can induce complete gene silencing in mammalian cells and primary cultures" Oligonucleotides. 13(5):381-92	
	127	Fedoriw A.M., et al. (2004) "Transgenic RNAi reveals essential function for CTCF in H19 gene imprinting" Science. 303(5655):238-40	
	128	Gan L., et al. (2002) "Specific interference with gene expression and gene function mediated by long dsRNA in neural cells" J Neurosci Methods. 121(2):151-7	
	129	Lazar, S. et al. (2004) "Selective degradation of cyclin B1 mRNA in rat oocytes by RNA interference (RNAi)" J Mol Endocrinol. 33(1):73-85	

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<b>Form PTO-1449 (Substitute) U.S. Department of Commerce Patent and Trademark Office</b>  <b>INFORMATION DISCLOSURE STATEMENT</b> <b>(Use several sheets if necessary)</b>	<b>Application Number</b>	10/759,841
	<b>Filing Date</b>	January 15, 2004
	<b>First Named Inventor</b>	Michael Wayne Graham
	<b>Art Unit</b>	1635
	<b>Examiner Name</b>	Whiteman, Brian A.
	<b>Attorney Docket No.</b>	0687/74768-AA /JPW/GJG/MJP

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	130	Stein P., et al. (2003) "Transgenic RNAi in mouse oocytes: a simple and fast approach to study gene function" Dev Biol. 256(1):187-93	
	131	Svoboda P., et al. (2004) "Lack of homologous sequence-specific DNA methylation in response to stable dsRNA expression in mouse oocytes" Nucleic Acids Res. 32(12):3601-6	
	132	Svoboda P., et al. (2004) "RNAi and expression of retrotransposons MuERV-L and IAP in preimplantation mouse embryos" Dev Biol. 269(1):276-85	
	133	Yi C.E., et al. (2003) "Specific and potent RNA interference in terminally differentiated myotubes" J Biol Chem. 278(2):934-9	
	134	Yu J., et al. (2004) "Transgenic RNAi-mediated reduction of MSY2 in mouse oocytes results in reduced fertility" Dev Biol. 268(1):195-206	
	135	Song J., et al. (2004) "Poly(U) and polyadenylation termination signals are interchangeable for terminating the expression of shRNA from a pol II promoter," Biochem Biophys Res Commun. 323(2):573-8	
	136	Clemens MJ. (1997) "PKR--a protein kinase regulated by double-stranded RNA," Int J Biochem Cell Biol. 29(7):945-9.	
	137	Dale et al. (2000) "A test of the model to predict unusually stable RNA hairpin loop stability" RNA 6 608-615	
	138	de Feyter R et al. (1996) "A ribozyme gene and an antisense gene are equally effective in conferring resistance to tobacco mosaic virus on transgenic tobacco" Mol Gen Genet. 250: 329-338	
	139	December 17, 2004 edition (2004) Biotechnol. News 24(30):1-12 (Yanicek, C., ed., CTB International Publishing, Inc., Maplewood, N.J., pub.)	
	140	Definition of "copy" (1995) Webster's New World Dictionary, p. 135, Neufeldt, V., and Sparks, A.N., eds., Simon & Schuster Inc., New York, NY	
	141	Definition of "palindrome" (1999) Glossary of biotechnology and genetic engineering, p. 172, Zaid, A., et al., eds., Food and Agriculture Organization of the United Nations, Rome, Italy	

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	<b>Filing Date</b>	January 15, 2004
	<b>First Named Inventor</b>	Michael Wayne Graham
	<b>Art Unit</b>	1635
	<b>Examiner Name</b>	Whiteman, Brian A.
	<b>Attorney Docket No.</b>	0687/74768-AA /JPW/GJG/MJP

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	142	Doelling JH and Pikaard CS (1995) "The minimal ribosomal RNA gene promoter of Arabidopsis thaliana includes a critical element at the transcription initiation site" Plant J. Nov;8(5):683-92.	
	143	Giering J.C., et al. (2008) "Expression of shRNA from a tissue-specific pol II promoter is an effective and safe RNAi therapeutic," Mol Ther. 16(9):1630-6	
	144	Gross, H.J., et al. (1982) "Nucleotide Sequence and Secondary Structure of Citrus Exocortis and Chrysanthemum Stunt Viroid," Eur. J. Biochem. 121(2):249-57	
	145	Huang Y and Carmichael G (1996) "Role of polyadenylation in nucleocytoplasmic transport of mRNA" Mol. Cell. Biol. 16: 1534-1542	
	146	Jacobs BL, Langland JO. "When two strands are better than one: the mediators and modulators of the cellular responses to double-stranded RNA," Virology (1996) 219(2):339-49.	
	147	Kim S & Wold BJ (1985) "Stable Reduction of Thymidine Kinase Activity in Cells Expressing High Levels of Anti-Sense RNA" Cell Vol. 42, 129-138	
	148	Kumar M and Carmichael G (1998) "Antisense RNA: Function and Fate of Duplex RNA in Cells of Higher Eukaryotes" Microbiol. Mol. Biol. Rev. 62(4): 1415-1434	
	149	Lodish et al. (c1999) "Molecular Cell Biology" Chapter 11, Section 11.2. (New York: W. H. Freeman & Co.).	
	150	Minks MA et al. (1979) "Structural requirements of double-stranded RNA for the activation of 2',5'-oligo(A) polymerase and protein kinase of interferon-treated HeLa cells" J. Biol. Chem. Vol. 254, No. 20: 10180-10183	
	151	Noonberg SB et al. (1994) "In vivo generation of highly abundant sequence-specific oligonucleotides for antisense and triplex gene regulation " Nucleic Acids Research Vol. 22 No. 14:2830-2836	
	152	Paul CP, Good PD, Winer I, Engelke DR. (2002) "Effective expression of small interfering RNA in human cells," Nat Biotechnol. 20(5):505-8.	
	153	Plasmid map for pCR2.1	

**EXAMINER  
SIGNATURE**
**DATE CONSIDERED**

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	<b>Filing Date</b>	January 15, 2004
	<b>First Named Inventor</b>	Michael Wayne Graham
	<b>Art Unit</b>	1635
	<b>Examiner Name</b>	Whiteman, Brian A.
	<b>Attorney Docket No.</b>	0687/74768-AA /JPW/GJG/MJP

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Examiner Initials <sup>*</sup>	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	154	Ramezani et al (1997) "Inhibition of HIV-1 replication by retroviral vectors expressing monomeric and multimeric hammerhead ribozymes" Gene Therapy 4 861-867	
	155	Ruiz F, Vayssié L, Klotz C, Sperling L, Madeddu L. (1998) "Homology-dependent gene silencing in Paramecium," Mol Biol Cell. 9(4):931-43.	
	156	Sachs A. and Wahle E. (1993) "Poly(A) tail metabolism and function in eucaryotes" J. Biol. Chem. 268: 22955-22958	
	157	Sánchez Alvarado A, Newmark PA. (1999) "Double-stranded RNA specifically disrupts gene expression during planarian regeneration," Proc Natl Acad Sci U S A. 96(9):5049-54.	
	158	Sijen et al., Post-transcriptional gene-silencing RNAs on the attack or on the defense?, 2000, BioEssays, 22: 520-513	
	159	Szyf et al. (1992) "Induction of Myogenic Differentiation by an Expression Vector Encoding the DNA Methyltransferase cDNA Sequence in the Antisense Orientation" J. Biol. Chem., 267:12831-12836	
	160	Tuschl T. (2002) "Expanding small RNA interference" Nat Biotechnol. May;20(5):446-8	
	161	Wallace RB et al. (1979) "Hybridization of synthetic oligodeoxyribonucleotides to phi chi 174 DNA: the effect of single base pair mismatch." Nucleic Acids Res.6(11):3543-57	
	162	Wu H et al. (1998) "Identification and Partial Purification of Human Double Strand RNase Activity" J Biol Chem, Vol. 273, Issue 5, 2532-2542	
	163	Yang, D., et al. (2000) "Evidence that processed small dsRNAs may mediate sequence-specific mRNA degradation during RNAi in Drosophila embryos," Curr. Biol. 10(19):1191-1200	
	164	Yu, J.Y., et al. (2002) "RNA interference by expression of short-interfering RNAs and hairpin RNAs in mammalian cells," Proc. Natl. Acad. Sci. USA 99(9):6047-52	

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# **EXHIBIT 46**

**Amendment As A Submission Under 37 C.F.R. § 1.114(c)**

Submitted: September 24, 2009

**Serial No. 10/759,841**

Filed: January 15, 2004

Applicants: Michael Wayne Graham et al.



Exhibit 46: Table of Locations for Disclosed Documents

Document	Document Description	Document Location
1	U.S. Patent No. 5,017,488 (McAllister et al.), May 21, 1991	Available to the Examiner on PAIR
2	U.S. Patent No. 5,270,163 (Gold et al.), December 14, 1993	Available to the Examiner on PAIR
3	U.S. Patent No. 5,457,189 (Crooke et al.), October 10, 1995	Available to the Examiner on PAIR
4	U.S. Patent No. 5,580,703 (Kotin et al.), December 3, 1996	Available to the Examiner on PAIR
5	U.S. Patent No. 5,707,835 (Haseloff et al.), January 13, 1998	Available to the Examiner on PAIR
6	U.S. Patent No. 5,795,715, issued August 18, 1998, to Thierry Livache et al.	Available to the Examiner on PAIR
7	U.S. Patent No. 6,344,316 B1, issued February 5, 2002 to David J. Lockhart et al.	Available to the Examiner on PAIR
8	U.S. Patent No. 6,995,258 (Rossietal et al.), February 7, 2006	Available to the Examiner on PAIR
9	U.S. Published Application No. 2003/0148519 (Engelke et al.), August 7, 2003	Available to the Examiner on PAIR
10	Amendment submitted June 12, 2008 in connection with U.S. Serial No. 11/593,056, filed November 6, 2006	Submitted June 12, 2008 in connection with U.S. Serial No. 11/593,056, filed November 6, 2006
11	Office Action issued September 12, 2008 in connection with U.S. Serial No. 11/593,056, filed November 6, 2006	Issued September 12, 2008 in connection with U.S. Serial No. 11/593,056, filed November 6, 2006
12	Advisory Action issued June 6, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Issued June 6, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
13	Advisory Action issued June 6, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Issued June 6, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
14	Amendment submitted May 11, 2009 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Submitted May 11, 2009 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
15	Amendment submitted September 2, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Submitted September 2, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005

Document	Document Description	Document Location
16	Amendment, including Exhibits A and B submitted May 21, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Submitted May 21, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
17	Communication submitted September 2, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Submitted September 2, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
18	Final Office Action issued August 13, 2009 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Issued August 13, 2009 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
19	Interview Summary for February 1, 2008 Interview in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Issued February 1, 2008 Interview in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
20	Office Action issued July 30, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Issued July 30, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
21	Office Action issued November 10, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005	Issued November 10, 2008 in connection with U.S. Serial No. 11/179,504, filed July 13, 2005
22	Amendment and Request for Continued Examination submitted January 7, 2009 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	Submitted January 7, 2009 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003
23	Final Office Action issued May 15, 2009 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	Issued May 15, 2009 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003
24	Notice of Improper Request for Continued Examination issued October 29, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	Issued October 29, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003
25	Office Action issued July 7, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	Issued July 7, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003
26	Request for Continued Examination submitted October 7, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003	Submitted October 7, 2008 in connection with U.S. Serial No. 10/346,853, filed January 17, 2003
27	Amendment submitted October 9, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	Submitted October 9, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004
28	Interview Summary for December 22, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	Issued December 31, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004

Document	Document Description	Document Location
29	Interview Summary for February 12, 2009 Interview in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	Issued February 20, 2009 Interview in connection with U.S. Serial No. 10/759,841, filed January 15, 2004
30	Office Action issued January 22, 2009 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	Issued January 22, 2009 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004
31	Office Action issued January 6, 2009 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	Issued January 6, 2009 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004
32	Office Action issued July 9, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004	Issued July 9, 2008 in connection with U.S. Serial No. 10/759,841, filed January 15, 2004
33	Amendment and Request for Continued Examination Submitted September 5, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	Submitted September 5, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004
34	Amendment submitted May 4, 2009 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	Submitted May 4, 2009 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004
35	Amendment, including Exhibits A to C submitted September 5, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	Submitted September 5, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004
36	Notice to the applicant regarding a non-compliant or non-responsive amendment issued September 4, 2009 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	Issued September 4, 2009 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004
37	Office Action issued November 3, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	Issued November 3, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004
38	Office Action issued September 2, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004	Issued September 2, 2008 in connection with U.S. Serial No. 10/821,726, filed April 8, 2004
39	Amendment submitted June 6, 2008 in connection with U.S. Serial No. 11/180,928, filed July 13, 2005	Submitted June 6, 2008 in connection with U.S. Serial No. 11/180,928, filed July 13, 2005
40	Amendment submitted February 7, 2008 in connection with U.S. Serial No. 10/821,710, filed April 8, 2004	Submitted February 7, 2008 in connection with U.S. Serial No. 10/821,710, filed April 8, 2004
41	Notice of Abandonment issued December 15, 2008 in connection with U.S. Serial No. 10/821,710, filed April 8, 2004	Issued December 15, 2008 in connection with U.S. Serial No. 10/821,710, filed April 8, 2004

Document	Document Description	Document Location
42	U.S. Published Application No. 2006/0014715, published January 19, 2006 (U.S. Serial No. 11/218,999, filed September 2, 2005; Michael Wayne Graham et al.), including complete file history	Available to the Examiner on PAIR
43	Amendment submitted June 17, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	Submitted June 17, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005
44	Amendment submitted March 30, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	Submitted March 30, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005
45	Communication issued May 21, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	Issued May 21, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005
46	Office Action issued May 21, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	Issued May 21, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005
47	Office Action issued September 30, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	Issued September 30, 2008 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005
48	Response to Communication submitted June 22, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	Submitted June 22, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005
49	Supplemental Response To March 30, 2009 Amendment Filed In Response To September 30, 2008 Office Action filed August 4, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005	Submitted August 4, 2009 in connection with U.S. Serial No. 11/218,999, filed September 2, 2005
50	Amendment submitted July 15, 2009 in connection with U.S. Serial No. 10/646,070, filed July 13, 2005	Submitted July 15, 2009 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003
51	Amendment submitted July 24, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003	Submitted July 24, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003
52	Amendment submitted May 11, 2009 in connection with U.S. Serial No. 10/646,070, filed July 13, 2005	Submitted May 11, 2009 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003
53	Amendment submitted October 10, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003	Submitted October 10, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003

Document	Document Description	Document Location
54	Amendment, including Exhibits A to I submitted July 24, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003	Submitted July 24, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003
55	Office Action issued November 4, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003	Issued November 4, 2008 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003
56	Office Action, issued June 9, 2009 in connection with U.S. Serial No. 10/646,070, filed July 13, 2005	Issued June 9, 2009 in connection with U.S. Serial No. 10/646,070, filed August 22, 2003
57	Office Action issued July 8, 2008 in connection with U.S. Serial No. 09/646,807, filed December 5, 2000	Issued July 8, 2008 in connection with U.S. Serial No. 09/646,807, filed December 5, 2000
58	Petition For Extension of Time submitted April 22, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Submitted April 22, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
59	Advisory Action issued April 24, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Issued April 24, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
60	Advisory Action issued March 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Issued March 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
61	Advisory Action issued March 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Issued March 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
62	Amendment after Final submitted February 26, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Submitted February 26, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
63	Amendment submitted July 11, 2008 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Submitted July 11, 2008 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively

Document	Document Description	Document Location
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65	Appeal Brief submitted July 27, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Submitted July 27, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
66	Decision on Petition For Extension of Time issued April 27, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Issued April 27, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
67	Decision on Petition Under 37 C.F.R. § 1.181 issued April 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Issued April 25, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
68	Declaration of Dr. Arthur Riggs Under 37 C.F.R. §1.132, including Exhibits A to I submitted February 26, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Submitted February 26, 2009 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively
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71	Office Action issued November 19, 2008 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively	Issued November 19, 2008 in connection with Merged Reexamination Nos. 90/007,247 and 90/008,096, filed October 4, 2004 and May 18, 2006, respectively

Document	Document Description	Document Location
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81	Pending claims for U.S. Serial No. 10/283,267, filed October 30, 2002	Available to the Examiner on PAIR
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92	Amendment submitted May 1, 2008 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	Submitted May 1, 2008 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999
93	March 18, 2009 Declaration Under 37 C.F.R. 1.131 including Annexes I to III, of Dr. Michael Metzloff in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	Submitted March 19, 2009 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999
94	May 1, 2008 Declaration Under 37 C.F.R. § 1.131, including Exhibits 1 to 5 of Peter Michael Waterhouse, Michael Wayne Graham, Ming-Bo Wang and Neil A. Smith in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	Submitted May 1, 2008 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999
95	May 7, 2008 Declaration Under 37 C.F.R. 1.132 of Peter Robert Schofield Resubmission in connection with U.S. Serial No. 09/287,632, filed April 7, 1999	Submitted May 7, 2008 in connection with U.S. Serial No. 09/287,632, filed April 7, 1999
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102	Declaration of Geoffrey Ellacott submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	Submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.
103	Declaration of Neil Smith submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	Submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.
104	Declaration of Peter Michael Waterhouse submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	Submitted April 15, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.
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106	Interview Summary from February 11, 2009 Interview in connection with U.S. Serial No. 11/364,183, filed March 1, 2006	Issued February 17, 2009 Interview in connection with U.S. Serial No. 11/364,183, filed March 1, 2006
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Document	Document Description	Document Location
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110	Supplemental Response or Supplemental Amendment submitted August 10, 2009 in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.	Submitted August 10, 2009, in connection with U.S. Serial No. 11/364,183, filed March 1, 2006.
111	Amendment submitted January 30, 2009 in connection with U.S. Serial No. 11/607,062, filed December 1, 2006	Submitted January 30, 2009 in connection with U.S. Serial No. 11/607,062, filed December 1, 2006
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113	Office Action issued May 12, 2009 in connection with U.S. Serial No. 11/607,062, filed December 1, 2006	Issued May 12, 2009 in connection with U.S. Serial No. 11/607,062, filed December 1, 2006
114	Amendment submitted January 16, 2008 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007	Submitted January 16, 2008 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007
115	Amendment submitted July 6, 2009 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007	Submitted July 6, 2009 in connection with U.S. Serial No. 11/841,737, filed August 20, 2007
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